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The place of goal-directed haemodynamic therapy in the 21st century

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Key points

- Goal-directed haemodynamic therapy (GDT) describes a complex bundle of care used perioperatively in high-risk adult surgical patients and for adults with sepsis.
- Through various combinations of fluids, oxygen, and vasoactive drugs, total blood flow and calculated tissue oxygen delivery are augmented with the aim of improving patient outcome.
- Haemodynamic monitoring (either invasive or minimally invasive) is required.
- GDT significantly reduces the duration of hospital stay and overall postoperative complication rate, specifically postoperative kidney injury, respiratory failure, and wound infection.
- The impact of GDT on mortality remains uncertain. Adequately powered pragmatic multicentre trials into GDT are therefore justified.

This article will discuss the history and subsequent development of goal-directed haemodynamic therapy (GDT), reviewing briefly the significant clinical trials of GDT, and finally suggest a practical clinical guide to GDT based on the most up-to-date evidence synthesis. The future role for GDT will also be discussed.

The high-risk surgical patient

The 'high-risk' surgical patient may be classified in a variety of ways. One suggested threshold includes those patients who have an individual postoperative mortality risk exceeding 5%, incorporating surgical factors such as complexity and urgency (often emergency), and patient factors such as comorbidities and (increasing) age.[1] 'Extremely high-risk' patients are those whose postoperative mortality risk is ≥20%.[2] Another classification describes those patients undergoing procedures that carry an inherent mortality rate exceeding 5%. Twenty-five per cent of the surgical population undergoing vascular, upper gastrointestinal, lower gastrointestinal, and hepatobiliary surgery fall into this latter category.[3]

Measures of cardiovascular fitness can also be used to stratify patient risk. Patients unable to achieve four metabolic equivalents (METS) (such as climbing a flight of stairs or gardening) are designated high risk, as are those with an anaerobic threshold (AT) of ≤11 ml of oxygen per kilogram per minute (ml O_2 kg^{-1} min^{-1}) on preoperative cardiopulmonary exercise testing (CPET). High-risk surgical patients account for 12.5% of surgical activity and yet this group accounts for 80% of postoperative deaths. However, ≤15% of high-risk surgical patients are electively admitted to critical care in the UK.[1]

Goal-directed haemodynamic therapy

GDT describes a complex bundle of care used perioperatively in high-risk adult surgical patients, and for adults with acute severe sepsis or septic shock. Total blood flow and tissue oxygen delivery are augmented through the use of various combinations of supplemental fluids, vasoactive drugs (inotropes, vasopressors, and vasodilators), and oxygen, with the aim of improving patient outcome. Although initially developed in critical care for use in high-risk surgical patients with shock, GDT is also now used in general surgical, orthopaedic, cardiothoracic, and vascular surgery.

Historically, empirical perioperative haemodynamic goals have been set and the effects of specific interventions assessed using information on blood flow gained from a cardiac output (CO) monitor. Originally, a pulmonary artery (right heart) catheter was required to measure haemodynamic variables using thermodilution techniques. Now different measurement modalities exist which have been well validated. The most widely used technologies include oesophageal Doppler monitoring (CardioQ-ODM™, Deltex Medical Ltd, UK) and arterial pulse contour analysis devices such as LiDCO™ (LiDCO Ltd, UK), PiCCO (PULSION Medical Systems SE, Germany), and the FloTrac Sensor/Vigileo monitor system (Edwards Lifesciences Corporation, USA).

A number of approaches have been suggested for the optimization of haemodynamic variables in the perioperative period and in patients with critical illness. Monitoring of pulse pressure or systolic pressure variation in the arterial pressure trace has been used as a means of predicting fluid responsiveness.[4] Stroke volume (SV) variation derived from a CO monitor has also been used in this way. The 'holy grail' of using tissue perfusion monitoring as a means of guiding haemodynamic management is often suggested, and was partially evaluated in studies of gastrointestinal tonometry,[5–7] but as yet no perfusion monitor has been effectively used in this way. The properties of the 'ideal' haemodynamic monitor are shown in Table 1. An in-depth review of all the available technologies is beyond the scope of this article.

The most frequently targeted haemodynamic variables include CO, SV [from which oxygen delivery (DO_2) and oxygen consumption (VO_2) can be calculated], and systemic vascular resistance. These variables may then be indexed to body surface area (average values being 1.9 m^2 for men and 1.6 m^2 for women) to enable comparison of the individual's measured values against a specified haemodynamic goal. Related target variables that are measures of the balance between oxygen delivery and oxygen utilization have also been studied and include mixed venous oxygen saturation SVO_2, oxygen extraction ratio (O_2ER), and blood lactate.

GDT has had a controversial history, some of which is due to the fact that it is a 'complex intervention' with multiple interacting components and also that the early studies of GDT required placement of a pulmonary artery catheter (PAC) in a critical care environment. More recent studies however have used less invasive devices and not mandated critical care admission as part of the intervention.

Table 1 Properties of an 'ideal' haemodynamic monitoring system (adapted from Vincent and colleagues[8])

Accurate and reproducible measurement of relevant haemodynamic variables
Rapid response time
Operator-independent equipment
Derived information can readily be used to guide therapies
Easy to use
Causes no harm to patients
Cost-effective

The theory

It is well established that oxygen consumption increases perioperatively. The magnitude of this change varies, but one study of 100 elderly patients undergoing elective major abdominal surgery reported an average increase of 44%, and others have reported increases of more than 50% in some instances.[9] This increased metabolic demand requires an increase in oxygen delivery that the patient may not be able to achieve through a spontaneous increase in CO.[10,11] The increased metabolic demand caused by major surgical trauma, when coupled with inadequate resuscitation and organ hypoperfusion, is strongly implicated in the development of postoperative multiple organ failure (MOF).

Tissue hypoxia is central to the development of postoperative MOF,[11] and its incidence is increased in high-risk patients with limited cardiovascular reserve. The hypothesis behind GDT is that augmentation of CO and oxygen delivery leads to improved tissue perfusion and oxygenation, thereby preventing the development of MOF. This in turn should confer a survival benefit resulting in high-risk patients undergoing major surgery experiencing fewer postoperative complications. Through optimization of SV and low-dose inotropy (dopexamine), Jhanji and colleagues[12] demonstrated that sublingual and cutaneous microvascular flow and cutaneous tissue oxygen partial pressure can be significantly increased after major gastrointestinal surgery.

Background

Interest and research into GDT followed the publication of the first use of the 'flow-directed balloon-tipped pulmonary artery (right heart) catheter' in humans by Swan and colleagues in 1970.[13] Before this, the use of the Fick principle to determine CO had been possible in the laboratory setting but was not routinely performed at the bedside in critically unwell patients.

The pulmonary artery catheter

The first description of right heart catheterization to aid diagnosis in critically unwell patients was by Bradley[14] in 1964 at St Thomas' Hospital, London. Until that time, right heart catheterization had only been used in patients with cardiac valvular disease and congenital heart disease. Using the Seldinger technique,[15] Bradley advanced miniature cardiac catheters from the basilic vein (or a branch thereof) in the antecubital fossa, subsequently taking pressure recordings in the right atrium, right ventricle, and pulmonary artery using a manometer. Four years later, Branthwaite and Bradley[16] (again at St Thomas') published the first paper describing right heart catheterization in humans using thermodilution to measure CO. The technique involved the use of a thermistor mounted in the tip of the catheter to detect the change in temperature of blood in a pulmonary artery after the injection of 10 ml of room temperature 5% dextrose or 0.9% saline into the right atrium (injected via a second catheter placed in the internal jugular vein). The CO measurements obtained were validated against the direct Fick technique, the method used previously to determine CO.

Swan and colleagues[13] added an inflatable latex balloon just proximal to the tip of a dual-lumen catheter in 1970 (major and minor lumens with the minor lumen being connected to the balloon). Inflation of the balloon allowed for the consistent (and safer) progression of the catheter through the heart and the

great vessels and also afforded the measurement of pulmonary artery wedge pressure (an indirect measure of left atrial pressure). Again this catheter was inserted via a vein in the antecubital fossa and did not require fluoroscopy to guide placement, so could be positioned at the bedside in critically unwell patients. Early modifications included positioning a thermistor at the tip (akin to Branthwaite and Bradley), thereby allowing measurement of CO by thermodilution.

The controversy of the PAC

In its initial stages, GDT required a PAC to calculate the haemodynamic data. Unfortunately, concerns about PAC safety followed and the publication of a large cohort study suggested that PAC use was associated with increased mortality and increased use of critical care resources.[17] Naturally, this attracted substantial interest and as a result PACs, and with them GDT, fell out of favour. More recent randomized controlled trials (RCTs)[18–20] have failed to demonstrate significant evidence for either benefit or harm when using a PAC to guide therapies perioperatively or in critical care. Interest in GDT has been re-invigorated however with the advent of newer minimally invasive devices that provide haemodynamic monitoring without the risks inherent with the PAC. An obituary for the PAC was written in 2013,[21] but it is still commonly used in some clinical environments including cardiac surgery and cardiac intensive care.

William Shoemaker

Using the PAC to measure haemodynamic variables, Shoemaker and colleagues[22,23] (Los Angeles, USA) were the first to describe the physiological patterns in surviving and non-surviving postoperative patients with shock secondary to surgical and accidental trauma. They found that patients who survived maintained higher physiological indices after operation [such as cardiac index (CI) and oxygen consumption (VO_2)] than those who died, and that this was associated with shorter periods of circulatory shock. Shoemaker and colleagues went on to suggest that therapy in this high-risk population should be aimed not at restoring normal physiological variables as had been previously thought, but at achieving higher than normal, 'supranormal', haemodynamic indices postulating that this would serve to meet the higher postoperative metabolic demands.

Goal-directed therapy literature

The first prospective trial evaluating GDT in high-risk surgical patients was by Shoemaker and colleagues in 1988.[24] The investigators, guided by measurements taken using a PAC, used fluids (crystalloids, synthetic colloids, and packed red cells), vasoactive drugs, and supplemental oxygen to achieve their GDT aims (although oxygen was not explicitly described as being part of the therapeutic intervention). The GDT goals sought in the protocol group are listed in Table 2.

The GDT group, in whom therapies were initiated before operation, achieved an average DO_2I>600 ml min^{-1} m^{-2} in the postoperative period and had significantly reduced: number of days on intensive care, number of ventilator days, number of postoperative complications, and number of postoperative deaths. Although this was an enthusiast-led, single-centre trial, and therefore had a high risk of bias, the evidence was compelling enough that subsequent trials have sought to build on these findings.

Table 2 Shoemaker and colleagues[24] GDT targets

Haemodynamic goal	Comparison with normal
CI>4.5 litre min^{-1} m^{-2}	50% greater
DO_2I>600 ml min^{-1} m^{-2}	At least 10% greater
VO_2I 170 ml min^{-1} m^{-2}	30% greater

PAC literature

In the UK, papers by Boyd and colleagues[25] and Wilson and colleagues[26] both reported significant reductions in morbidity and mortality in high-risk surgical patients where CI and oxygen delivery were augmented perioperatively using fluids, oxygen, and dopexamine, guided by a PAC. Wilson[26] also demonstrated significant reductions in length of stay (Boyd and colleagues[25] also showed that the GDT group tended to spend less time in intensive care and had a shorter hospital stay, although this was not statistically significant). But whereas Boyd and colleagues[25] admitted all patients to intensive care postoperatively, Wilson and colleagues[26] have been criticized because although patients in their intervention group routinely went to critical care, many patients in their control group were cared for postoperatively on the ward.

Not every trial into PAC-guided GDT has demonstrated its benefit. Studies into patients with established critical illness have demonstrated that such an intervention is associated with either no difference between groups or in some cases harm in the intervention group, suggesting that the timing of GDT during the clinical course is important.

In a prospective RCT of mixed critical care patients, and again using dobutamine, Hayes and colleagues[27] found that despite achieving significantly higher CI and DO_2I (but surprisingly lower oxygen extraction) in the protocol group, in-hospital mortality was in fact significantly lower in the control group. The authors suggested that good physiological reserve (and perhaps a less severe illness) conferred a survival benefit, as patients in the control group were able to achieve the GDT indices with fluids alone. However, whereas Shoemaker and others have instituted therapy before operation, this study included mainly postoperative surgical patients and those with established critical care illnesses such as acute respiratory failure and septic shock.

In the largest negative PAC GDT trial to date, Gattinoni and colleagues[28] were unable to demonstrate a significant difference in mortality, organ dysfunction, or length of stay on intensive care between the protocol and control groups. In this trial, SVO_2 was also evaluated as a target for GDT (and also CI), as it represents the balance between oxygen consumption and oxygen delivery. Interestingly, significantly fewer patients in the CI group were able to achieve their targets compared with the control group and significantly fewer of the older and sicker patients were able to meet their respective goals, suggesting again the influence of premorbid cardiovascular function on the effectiveness of GDT.

Non-PAC literature

Although originally closely associated with the PAC, a distinct parallel GDT literature derives from the use of less invasive monitors such as lithium indicator dilution and arterial pulse contour analysis (LiDCO™) and oesophageal Doppler monitoring.

Using oesophageal Doppler monitoring-guided GDT and gastric tonometry to assess gastric mucosal pH (pHi—used as a marker of gut and therefore global hypoperfusion/hypovolaemia), Mythen and Webb[5] demonstrated a significantly lower incidence of gut mucosal hypoperfusion in the GDT group, which in turn was associated with significantly reduced postoperative major complication rate, average number of intensive

care days, and average number of hospital days. This association between pHi and outcome echoed previous work.[29]

Pearse and colleagues[30] published the first RCT looking specifically at *postoperative* GDT. Using LiDCO™ to guide therapies (including dopexamine) aimed at increasing oxygen delivery, the researchers demonstrated significant reductions in the number of complications per patient, the total number of complications, and the length of hospital stay in the protocol patients. There was also a 41% cost reduction in overall hospital stay associated with the GDT patients.

Again not every non-PAC GDT study has demonstrated benefit. Challand and colleagues[31] used the oesophageal Doppler to guide intraoperative GDT with colloid in patients undergoing colorectal surgery, stratified into being either aerobically 'fitter' (AT>11.0 ml O_2 kg^{-1} min^{-1}) or 'less fit' (AT 8.0–10.9 ml O_2 kg^{-1} min^{-1}) on the basis of preoperative CPET. Each group was then randomized into receiving standard therapy or GDT. Results showed that GDT did not improve time to readiness for discharge, nor overall length of hospital stay. And in a subgroup analysis, the 'fitter' GDT subgroup had a significantly increased median time until they were ready for discharge and a significantly prolonged length of stay. Interestingly, the GDT group also had significantly more intraoperative blood loss.

Finally, the largest UK multicentre RCT into haemodynamic optimization by Pearse and colleagues[32] has recently been published. 'OPTIMISE' (ISRCTN04386758) compared usual therapy *vs* minimally invasive CO monitor-guided GDT using a LiDCOrapid™ (LiDCO Ltd, UK) in high-risk patients undergoing major gastrointestinal surgery. The intervention period extended from the induction of anaesthesia until 6 h after operation. The haemodynamic therapy algorithm group received 250 ml colloid boluses to achieve a sustained increase in cardiac SV plus a fixed-dose infusion of dopexamine in order to optimize oxygen delivery (this GDT algorithm having previously been evaluated).[12]

On its own, the study failed to demonstrate a significant difference between the treatment and protocol groups in either primary (moderate and major complications and 30 day mortality) or secondary [POMS (Postoperative Morbidity Survey)-defined morbidity on day 7, infectious complications, critical care-free days, and all-cause mortality at 30 days after surgery] outcome measures. However, when the results are included in an updated systematic review and meta-analysis, they suggest that GDT significantly reduces the number of postoperative infections and length of hospital stay, which is consistent with the evidence summary reported in the Cochrane review by Grocott and colleagues[33] in 2012 (discussed below).

Sepsis

The first RCT looking specifically at GDT in early sepsis was by Rivers and colleagues[34] in 2001. Patients with severe sepsis or septic shock were randomized to receive either standard therapy or early goal-directed therapy (EGDT) in the emergency department of an inner city tertiary-level hospital for at least 6 h after presentation (and before admission to critical care).

In keeping with previous studies into GDT, synthetic fluids, packed red cells, and vasoactive drugs were used to attain haemodynamic targets (antimicrobial therapy was given to both groups at the discretion of the treating clinicians). Although only a single-centre trial and only partially blinded (therefore open to bias), the EGDT group had significantly lower in-hospital mortality, 28 and 60 day mortality. The duration of hospital stay was also significantly longer in patients receiving standard therapy who survived to discharge.

These results echoed previous studies in that GDT appeared to be of benefit if it is instigated early in the development of a critical illness, and the Rivers EGDT protocol subsequently formed the basis of the Surviving Sepsis Campaign initial resuscitation recommendations when managing severe sepsis and septic shock.[35]

More than a decade after the Rivers trial, however, three further multicentre trials have now recently been published investigating the validity of EGDT in the management of early sepsis. Their results differ from the Rivers trial in that neither the North American Protocol-Based Care for Early Septic Shock (ProCESS) trial,[36] the UK Protocolised Management in Sepsis (ProMISe) trial,[37] nor the Australasian Resuscitation in Sepsis Evaluation (ARISE) trial[38] were able to demonstrate a significant survival benefit for protocol-based EGDT over usual care at 90 days. All three studies concluded that EGDT did not confer a survival benefit in the management of patients admitted to the emergency department with early septic shock. As the ProMISe authors comment though, it may be that usual resuscitation techniques have evolved sufficiently since the Rivers trial that the extra benefit shown by EGDT previously would now not be seen.

Systematic reviews and meta-analyses

Studies into GDT have provided evidence both for and against its use and there have been a number of systematic reviews and meta-analyses performed to determine whether GDT is beneficial.[39–42] There is significant heterogeneity in the trials themselves, for example, in the population studied, the haemodynamic goals targeted, and the techniques used to achieve those goals, and in the approaches to meta-analysis used in the reviews.

A recent Cochrane review by Grocott and colleagues[33] explicitly reviewing the effects of perioperative GDT on postoperative outcome is the most rigorous to date. From an original electronic search yielding 10 462 studies, a total of 31 RCTs met the inclusion criteria (containing a total of 5292 patients). Based on their analyses, GDT did not significantly improve either overall mortality (at longest follow-up—the primary outcome) or hospital/28 day mortality (a secondary outcome) when compared with control (targeting explicit goals that were less than the intervention, as opposed to 'usual care'). This is contrary to previous meta-analyses that had shown mortality benefit with GDT.[39–42] However, the Cochrane mortality results were sensitive to methods of analysis, with several approaches resulting in a statistically significant improvement in mortality, suggesting uncertainty about the no-difference conclusion. Notwithstanding this, GDT was shown to reduce the postoperative incidence of kidney injury, respiratory failure, and wound infections, as well as the overall postoperative complication rate. For every 100 patients treated with GDT, an extra 13 will avoid a complication, two will avoid renal impairment, five will avoid respiratory failure, and four will avoid a postoperative wound infection when compared with control. GDT was also shown to significantly reduce the postoperative length of stay in hospital, though not the postoperative length of stay in critical care. Importantly, there was no evidence of harm associated with GDT.

GDT was shown to significantly reduce the mortality in elective surgery, however, when compared with urgent or emergency surgery, although there was no correlation with type of surgery, be it general, vascular, or cardiac. There was very limited data relating to patients undergoing emergency surgery. Interestingly, postoperative mortality was also not significantly affected by:

(i) the timing of GDT (be it preoperatively, intraoperatively, or postoperatively),
(ii) the type of therapy used (fluids alone or in combination with vasoactive drugs),
(iii) the haemodynamic goal targeted (be it CO and oxygen transport, SVO_2, or O_2ER and lactate).

Long-term outcome

Although shown to significantly reduce postoperative complications (and short-term mortality in elective surgery), the question remains: is there a signal that GDT can affect long-term outcome or is overall survival purely down to the original disease process? In the only long-term study of its type, Rhodes and colleagues[43] have attempted to answer this question by following-up patients from a study by Boyd and colleagues[25] in 1993 (described above) in which the patients in the protocol group received GDT targeting a DO_2I of 600 ml min^{-1} m^{-2}. At the time of randomization, both the control and protocol groups had been well balanced in terms of patient characteristics, type (and urgency) of surgery, and comorbidities. Outcome data were available in all but one of the original 107 patients.

Fifteen years post-randomization patients in the protocol group showed significantly improved survival with the median survival increased by over 3 yr and more than twice as many survivors in the protocol group than the control group (11 *vs* 4 patients). The avoidance of a postoperative complication had also conferred a significant survival advantage. And even in those patients who did develop a postoperative complication, GDT appeared to improve long-term survival. Development of cardiovascular or renal complications had the greatest (negative) impact on long-term survival.

Economic impact

Intensive Care National Audit and Research Centre (ICNARC, UK) data demonstrate that even though mortality from critical illness is decreasing, the number of adults requiring admission to critical care is increasing. So even though GDT has been shown to reduce postoperative complication rates and increase long-term survival in high-risk surgical patients, is it cost-effective in terms of additional resources (especially critical care resources), training, and maintenance of the new devices required for its implementation?

Ebm and colleagues[44] have recently undertaken a cost-effectiveness analysis of GDT to determine the implications of using GDT after operation for all high-risk surgical patients as opposed to providing usual care. The authors constructed two decision tree models: one analysing the costs and benefits in the short term (those relating to the hospital in the first 28 postoperative days), the other for the long term (those relating to society). The short-term model was developed based on the results of a previous study by Pearse and colleagues[30] (albeit only a single-centre study) and the long-term model simulated a hypothetical 67-yr-old patient using follow-up data from a separate publication by Rhodes and colleagues[43] (the only long-term GDT follow-up study, as described above).

Ebm and colleagues[44] found that GDT increased quality-adjusted life expectancy and provided healthcare savings to both the hospital and society. Specifically, in the short term, GDT was found to be more efficient and cost less than usual care, with a cost-reduction of £2631.77 per patient (£2134.86 per hospital survivor). Even accounting for maximum prolonged hospitalization and complications, GDT provided a cost saving of £471.65 per patient. An initial investment for two GDT monitors and training of staff cost £40 386.75, which would be offset after treating only 16 patients. This equates to GDT making savings after only 1.8 months (based on an average of 100 patients utilizing GDT over the course of the year).

In the long term, GDT was associated with an increased quality-adjusted life expectancy of 0.82 yr, lifetime cost savings of £1542.16 per patient (a 10% cost reduction compared with usual care, due to reduced hospital length of stay and decreased likelihood of developing complications), and a 99% probability for healthcare providers that GDT was cost-effective and thus the optimal choice for high-risk surgical patients.

A perioperative GDT algorithm for patients undergoing major non-cardiac surgery

It is unclear whether the original Shoemaker GDT values as described above are still appropriate today. Modern GDT management is concentrated on correcting hypovolaemia, using a haemodynamic monitor to target changes in SV. Once the patient is deemed 'volume replete', attention can then be turned to augmenting CO and with it maximizing oxygen delivery, with or without the use of vasoactive drugs.

Optimizing SV

Using information gleaned from a haemodynamic monitor, increases in SV, and therefore CO, are achieved initially through fluid challenges, typically consisting of 250 ml of either crystalloid or colloid. By convention, in GDT, an SV increase of ≥10% after a fluid challenge indicates that the patient is 'volume dependent' or 'volume deplete' and further fluid boluses are required to optimize ventricular performance. This is seen at point A in Figure 1 where an increase in end-diastolic volume (ΔV) after a fluid challenge results in an increased SV. This is because on the ascending portion of the Frank–Starling curve, an increased end-diastolic volume causes increased ventricular wall stretch and thus an increased force of cardiac contraction is developed[45] (positive inotropy).

If the SV increases by <10% after a fluid challenge then the patient is termed 'volume independent' or 'volume replete' and further fluid challenges (at that clinical time point) are not required

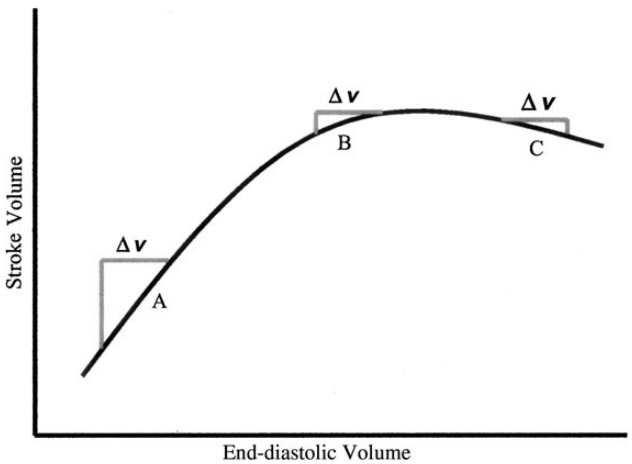

Fig 1 Adapted from the Frank–Starling law of the heart and depicts the relationship between SV and end-diastolic volume (or intravascular volume) for the human cardiac ventricle. (Taken from Grocott and colleagues[46] with kind permission from Lippincott Williams and Wilkins/Wolters Kluwer Health.)

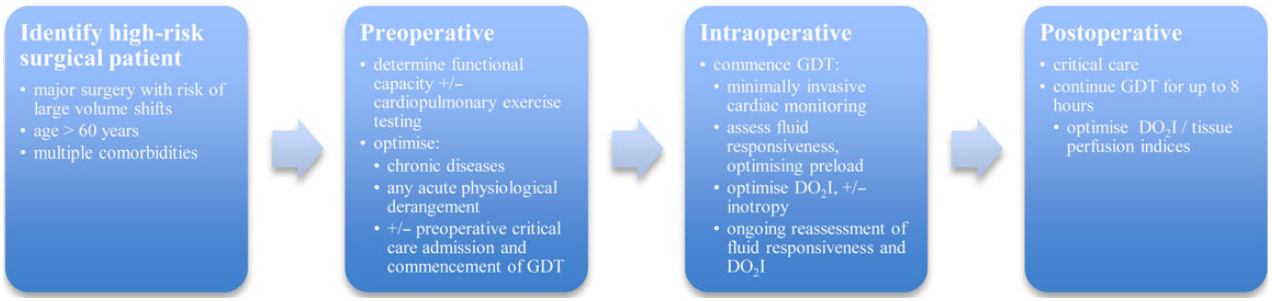

Fig 2 Suggested algorithm for the perioperative management of high-risk surgical patients (adapted from Lobo and de Oliveira[48] and Lees and colleagues[49]).

to improve ventricular performance. This is demonstrated by point B. Finally, if the SV decreases after a fluid bolus, then this is indicative of a decrease in ventricular performance due to ventricular overdistension. This is seen at point C and the patient may be at risk of ventricular failure and pulmonary oedema. It is important to remember that the Frank–Starling curve is in fact a family of curves, the position of which on each axis is dependent on the afterload and state of inotropy. Decreased afterload and increased inotropy shift the curve up and left (increasing SV), the opposite occurring with increased afterload and decreased inotropy.

Augmenting CO and oxygen delivery

Once SV has been optimized, CO (and with it systemic oxygen delivery) can be increased through the use of blood transfusions, oxygen, and vasoactive drugs (typically inotropes). The most frequently studied inotrope in GDT literature is the dopamine analogue dopexamine, a β-adrenergic (β_2) and dopaminergic (DA1 and DA2) agonist. The perioperative use of low-dose dopexamine (≤ 1 μg kg^{-1} min^{-1}) in high-risk surgical patients undergoing major surgery has been associated with decreased length of stay and a reduced 28 day mortality.[47] Dopexamine doses ≥ 1 μg kg^{-1} min^{-1} have failed to show any survival benefit however and are associated with detrimental side-effects such as tachycardia.

Although early studies into GDT have advocated achieving a DO_2I>600 ml min^{-1} m^{-2} for any surgical patient deemed high risk, as discussed by Lobo and de Oliveira,[48] DO_2I should perhaps be augmented on an individualized basis depending on the patient's preoperative values, the nature of surgery, and predicated VO_2I increase. Regardless, the aim of any DO_2I increase should be to keep DO_2 above baseline to reduce the likelihood of perioperative tissue hypoxia.[48] A suggested algorithm for perioperative GDT is shown in Figure 2.

Conclusion

The available evidence suggests that GDT has a role in the perioperative outcome of the high-risk surgical patient, by reducing the postoperative complication rate and the length of stay in hospital. However, the absolute mechanism for the benefit of GDT remains unclear.

A number of questions remain:

(i) When should GDT be commenced during the perioperative period? GDT was traditionally commenced in the preoperative period, but intra- and postoperative GDT has also shown benefit.
(ii) Which GDT technique should be used?
(iii) What types and quantities of fluids should be used?
(iv) Which haemodynamic monitoring device should be used? The PAC was previously the 'gold standard', but its use is controversial and has been superseded by newer technologies such as those described briefly above.
(v) Which vasoactive drug is preferential?
(vi) Is critical care admission an important component of the package?

Despite these questions, recent NICE guidance[50] stating that CardioQ-ODM™ oesophageal Doppler monitoring can be considered to guide intraoperative fluid therapy in higher risk patients where invasive cardiac monitoring was planned highlights the perceived benefits that optimizing CO and oxygen delivery has on patient outcome. Patient selection is clearly important, with 'fitter' patients and those with established disease less likely to benefit. Larger, adequately powered, pragmatic multicentre trials are justified to evaluate the effectiveness of perioperative GDT in routine clinical practice.

Supplementary material

Supplementary material is available at *BJA Education* online.

Declaration of interest

None declared.

MCQs

The associated MCQs (to support CME/CPD activity) can be accessed at https://access.oxfordjournals.org by subscribers to *BJA Education*.

Podcasts

This article has an associated podcast which can be accessed at http://www.oxfordjournals.org/podcasts/ceaccp_16.06.01.mp3.

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A complete list of references is available as Supplementary material.

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